logical deprivation of the sympathetic function by 6-OHDA administration was accompanied by a decrease of cAMP in the kidneys with RD to the control level.

The data obtained lead to the conclusion that the cause of aldosterone reception impairment under RD (as result of sympathetic hyperfunction) and an improvement of receptor function under pharmacological desympathization may be catecholamine-induced variations of cAMP, which switches on a protein kinase-initiated system of intracellular metabolism, yielded the alterations in the protein spectra of cytoplasm, nuclei, and chromatin in the rat tubule cells, including the aldosterone receptor complex and its molecular environment.

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Inotropic Responses of Human Myocardium in Ischemic Heart Disease

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Surgical management markedly improves the efficacy of treatment of ischemic heart disease (IHD), although it may be necessary to perform adjunct therapy by administering a fairly broad spectrum of pharmacological preparations [5]. This is all the more important, because surgical intervention may provoke heart dyskinesia and complicate the ischemic damage to the myocardium. At the same time, experimental results have been reported on a pronounced adaptogenic effect of brief repeated periods of ischemia or

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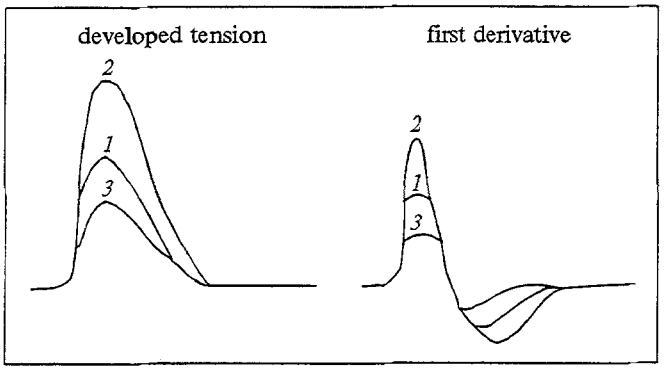

Fig. 1. Curves of single contraction of muscle preparation from human myocardium during short-term changes of stimulation frequency.1) basal frequency 0.5 Hz; 2) frequency reduced to 0.1 Hz; 3) frequency raised to 1 Hz.

hypoxia [9]. *In vitro*-obtained data provide evidence of altered Ca affinity of the contractile proteins [8], as well as of an increased resistance of the cellular structures to autolysis [10] in the ischemized myocardium.

In the present work the changes of contractility of a muscle preparation from a human myocardium biopsy specimen were investigated under the influence of different inotropic factors: changes of the stimulation frequency, the effect of a hypercalcium solution and epinephrine, and the combination of these factors.

MATERIALS AND METHODS

The study was carried out on trabeculae isolated from the auricle of the right atrium, which were obtained during the course of coronary bypass operation in patients with IHD, aged 40-55. The surgical specimen was placed in cooled Krebs-Henseleit solution [11]. After the necessary preparation, the trabeculae were fixed in a thermostabilized flow cell (volume 1 ml). The contractility was assessed isometrically at 31°C. After adaptation, the Ca^{2+} concentration in the perfusion fluid was increased from 2 to 4 mM in each of the 10 experiments performed (Ca test). After the maximum response to the Ca test was developed, the excess concentration of Ca^{2+} was washed out with a solution with a normal Ca^{2+} concentration until the initial level of contractility was attained. Then, 0.03-0.1 μM epinephrine was introduced into the solution. Before the Ca test, the stimulation frequency was changed from 0.5 to 0.1 and 1 Hz for a brief period at the maximum inotropic response and in the presence of epinephrine. The force of contractions and its first derivative were registered. The maximal developed tension (T_{max}) and the maximal velocity of tension rise (T'_{max}) and fall (T'_{min}) were calculated. The values of the parameters for each factor tested were expressed as % of the values obtained before the test.

RESULTS

A short-term increase or decrease of stimulation frequency was accompanied by a pronounced alteration of the contractility of the muscle preparation. A typical reaction observed for such an effect is presented in Fig. 1. Taking into account the similar organization of the processes in the cardiomyocytes of human beings and guinea pigs, one may expect a positive chronotropic response in our investigations, as described for the heart muscle of guinea pigs [12]. However, an increase of stimulation frequency from 0.5 to 1 Hz caused a negative inpotropic response: the developed tension, the velocity of its rise and fall reliably ($p<0.05$) decreased by 37% on the average. Conversely, a decrease of stimulation frequency from 0.5 to 0.1 Hz caused a reliable ($p>0.05$) positive inotropic response, the intensity of the changes of individual parameters being the following: T_{max} (20±4%) > T'_{min} (16±3%) > T'_{max} (13±4%).

The effect of the Ca^{2+} concentration in the physiological saline on the contractility of the muscle preparation from the human heart is presented in Fig. 2. An increase of the Ca^{2+} concentration from 2 to 4 mM caused a variously marked increase of the parameters of contractility and relaxation. For example, T'_{min} rose by 383% and was greater than T'_{max}, which rose by 324%; the T'_{max} augmentation was the weakest and constituted

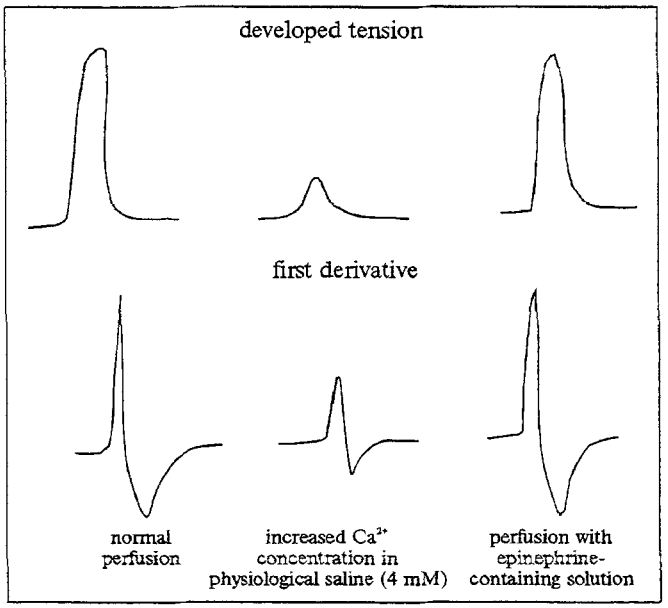

Fig. 2. Curves of single contraction of muscle preparation from human myocardium at a high external Ca^{2+} concentration and in the presence of epinephrine.

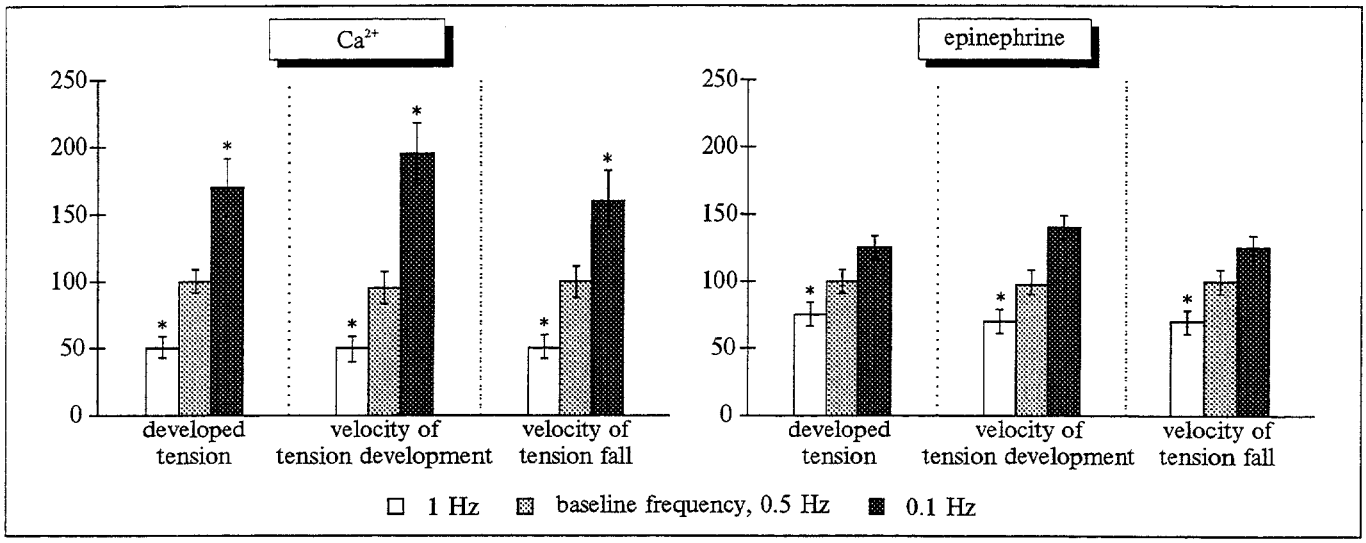

Fig. 3. Changes of contractility of muscle preparation from human myocardium during short-term shanges of stimulation frequency in the presence of 4 mM Ca^{2+} and epinephrine.

284%. Due to the preeminent increase of the velocity of fall of tension, the T'_{max}/T'_{min} ratio fell to 2.6 (vs. 3.3 at the initial level).

In our experiments, when epinephrine was added to the normal physiological saline, not only was an increase of the developed tension by 322% observed, equal to the effect of Ca^{2+}, but also the same response of the dynamic characteristics (T'_{max} rose by 255% and T'_{min} by 377%). The T'_{max}/T'_{min} ratio dropped to 2.7. The changes of the curve of developed tension and its first derivative in the presence of epinephrine are presented in Fig. 2.

An increase of stimulation frequency in the presence of a high Ca^{2+} concentration or of epinephrine caused a negative inotropic response (Fig. 3). Its intensity did not depend upon the previous effects. The decrease of all the parameters in question was reliable ($p<0.05$) and its average value was 35%, this being virtually equal to the effect of increased frequency observed before the Ca^{2+} concentration was raised or epinephrine was added to the perfusion fluid.

Lowering the stimulation frequency from 0.5 to 0.1 Hz caused an additional rise of the contractility of the muscle preparation in the presence of both 4 mM Ca^{2+} and epinephrine. As is shown in Fig. 3, against the background of the similar inotropic effects of a high Ca^{2+} concentration and epinephrine, a decrease of stimulation frequency exerted differently expressed effects. For instance, under such an influence, the increase of the developed tension was more pronounced in the presence of Ca^{2+}. In its presence, T'_{max} increased by 110±49% and the increment was reliably ($p<0.05$) higher than in the presence of epinephrine (38±9%). When the frequency was reduced, the increment of T'_{min} was also reliably higher (by 50%, $p<0.05$) than in the presence of 4 mM Ca^{2+}.

Thus, a decrease of stimulation frequency predominantly caused augmentation of the velocity of tension development both against the background of hypercalcium perfusion and in the presence of epinephrine, whereas under conditions of normal perfusion, a drop of stimulation frequency led to a preeminent increase of the amplitude of developed tension.

These findings are evidence of an altered nature of the rhythm-inotropic responses to changes of stimulation frequency and to the effects of β-agonists in the state of ischemia. At the same time, however, the functional reserve of the myocardium is still quite high. Such an effect may result from functional changes of the activity of the Ca pump in the sarcoplasmic reticulum [2,4] or of the enzymes participating in transmembrane ion transport, which change their activity in ischemia [6], as well as of possible rearrangements in the β-adrenergic structures [3]. The changes revealed can be considered a manifestation of the adaptive response of the myocardium functioning under the conditions of ischemia.

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Effect of High-Altitude Ecological and Experimental Stresses on the Platelet-Vascular Wall System

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Ecological stress is typically observed not only among people working in Antarctica, but also among those working in high mountains in Kyrgyztan [5,9]. In the mountains stress is induced by hypoxia, whose effect is heightened by cold. The neurohormonal indicator of high-altitude ecological stress (HES) is a twofold increase in the output of corticosteroids, the level of which returns to normal only after 30-45 days [4]. The stress is characterized by a hyperaggregation of platelets, which leads to an accumulation of thrombocytic (spontaneous) aggregates in the circulating blood and, eventually, to the occlusion of blood vessels [8]. Platelets resemble nerve cells, and are therefore convenient for testing the effect of ecological factors on the body and the pathophysiology of adaptation [10,11]. Prostacycline, an anticoagulant of the blood vessel wall (endothelium), behaves as a "counter-system" [2] with respect to platelets. The platelet and the vascular wall form a single functional system (PVWS), and homeostasis between them prevents thrombogenesis of the blood [3]. Under normal ecological conditions thrombogenesis is often caused by epinephrine and epinephrine-induced cardionecrogenic stress (ECNS) [1].

The purpose of the present work is to study the effect of high-altitude ecological and experimental stresses on the platelet-vessel wall system in animals and man.

MATERIALS AND METHODS

In experiments carried out on 64 white rats of both sexes weighing 200-250 g we determined the anticoagulant activity of the wall of the aorta (AAWA) [2,3,12], the index of spontaneous aggregation of platelets (SAP) [13], and the aggregation and disaggregation of platelets (AP and DP) [2]. The index of thrombophilia (TPh) was determined according to the formula (SAP/AAWA)×100 arbi-

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